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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,427	KIM ET AL.	
	Examiner	Art Unit	
	ALLISON M. FORD	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060913*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group III, claims 8-11 and 13, in the reply filed on 5/7/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-7 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-13 remain pending. Claims 8-11 and 13 have been considered on the merits.

Priority

Acknowledgment is made that the instant application is a national stage entry under 35 USC 371 of international application PCT/KR04/00054, filed 1/11/2005.

The international application appears to have made a priority claim to Korean application 10-2003-0002314, filed 1/14/2003. A certified copy of the Korean application has been received in the instant application from WIPO. However, the national stage of the instant application does not contain a proper claim to the foreign priority document under 35 USC 119(b) and 37 CFR § 1.55, as no reference is made in the declaration, or in an application data sheet, to the foreign application.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the foreign application for patent or inventor's certificate on which priority is claimed pursuant to 37 CFR 1.55, and any foreign application having a filing date before that of the application on which priority is claimed, by specifying the application number, country, day, month and year of its filing.

It appears the declaration submitted 3/9/2006 erroneously claimed foreign priority, under 35 USC 119(a)-(d) to the international application PCT/KR04/00054, instead of to the Korean application 10-2003-0002314. The error can be corrected by supplying an application data sheet in accordance with 37 CFR § 1.76(c).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is directed to a method of preparing a biological tissue; however the steps of claim 8 are not clear and thus render the claims indefinite.

Specifically, in the step of "adding a semi-permeable agent and cross-linking agent to the molding container and forming a semi-permeable membrane on an outer surface of each of the scaffolds loaded in the molding container to interconnect the scaffolds" is unclear.

First, "semi-permeable agent" is not an art recognized term, and there is no clear definition provided in the specification. It is noted that claim 9 recites the semi-permeable agent may be alginates, polysaccharides, chitosans, agar powder or gelatin, but it is not clear how each of these agents are semi-permeable, they are individual compounds, not materials that may or may not have permeability. Clarification is required.

Second, it is unclear how the semi-permeable membrane is formed on an outer surface of each of the scaffolds. The claim is understood to require a plurality of cell-seeded scaffolds to be loaded into a single container, if the scaffolds are already loaded into the container it would not appear that each of the scaffolds have an exposed surface to which a semi-permeable membrane can be applied. Furthermore, it is unclear how the semi-permeable membranes are situated on each of the scaffolds such that it interconnects the scaffolds. Again, if the scaffolds are pre-loaded into a single container, it would appear they would be interconnected by their close proximity. Thus, it is generally unclear of the spatial relationship between the scaffolds and the semi-permeable membranes.

Third, it is unclear what the semi-permeable membranes are semi-permeable *to* (*i.e.* nutrients, gas, cells, etc). Clarification is required.

Furthermore, the step of "introducing nutrients into the scaffolds interconnected with the cross-linking agent" is unclear. Previously the claim states that the semi-permeable membrane interconnects the scaffolds, not the cross-linking agent; thus there is not proper antecedent basis for "the scaffolds interconnected with the cross-linking agent".

The specification at page 11 states the semi-permeable membrane is formed by the action of the cross-linking agent on the 'semi-permeable agents'. The claim does not make this step clear as there is no correlation between the semi-permeable agent, the cross-linking agent and the semi-permeable membrane. Also, it is noted that gelatin, one of the disclosed species of semi-permeable agents, is not chemically cross-linked, thus it is unclear how the species of gelatin relates to the independent claim.

Finally, it is noted the preamble states the method is intended to prepare a biological tissue; however, the claim never recites that the biological tissue is ultimately created. It is noted the final line of the claim recites "thus proliferating the tissue cells"; however, it would be

remedial to recite "thus proliferating the tissue cells to produce a biological tissue", in order to make clear the recited steps carry out the intended method.

The dependent claims inherit the deficiencies of independent claim 8, and thus are rejected on the same grounds.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by Bader (US Patent 7,354,764) (filed as international application PCT/EP03/08325 on 7/28/2003).

Claim 13 is determined to be a product-by-process claim. Product-by-process limitations are considered only insofar as the method of production imparts distinct structural or chemical characteristics or properties to the product. Therefore if the product, as claimed, is the

same or obvious over a product of the prior art (*i.e.* is not structurally or chemically distinct), the claim is considered unpatentable over the prior art, even though the prior art product is made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), and *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

In the instant case, claim 13 is directed to a biological tissue prepared by the method of claim 8; when taking into consideration the steps of the method of claim 8, the product of claim 13 must include living cells seeded onto a at least one scaffold, and include a material that functions as a 'semi-permeable membrane' one at least one outer surface of the at least one scaffold. It is noted no specific size or form is required by the method of claim 8, and thus the tissue of claim 13 is not limited in size or form.

Bader is considered to anticipate the claims to the biological tissue of claim 13, as Bader discloses a construct, comprising cells seeded onto a support structure (which is the same as a scaffold), and the cell-seeded support structure encapsulated by a 'boundary layer'. The 'boundary layer' may be a hydrogel, and specifically alginate cross-linked via exposure to calcium chloride (See Bader, col. 1, ln 25-col. 2, ln 2 & col. 3, ln 65-col. 4, ln 2 & Fig. 5); thus the cross-linked alginate boundary layer reads on what Applicants call a semi-permeable membrane on at least one outer surface of the support structure (scaffold). Because the construct contains living cells, it is considered to be a 'biological tissue'. Therefore the reference anticipates the claimed subject matter.

Claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by Zaleske et al (US Patent 6,183,737).

Claim 13 is determined to be a product-by-process claim. Product-by-process limitations are considered only insofar as the method of production imparts distinct structural or chemical characteristics or properties to the product. Therefore if the product, as claimed, is the

same or obvious over a product of the prior art (*i.e.* is not structurally or chemically distinct), the claim is considered unpatentable over the prior art, even though the prior art product is made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), and *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

In the instant case, claim 13 is directed to a biological tissue prepared by the method of claim 8; when taking into consideration the steps of the method of claim 8, the product of claim 13 must include living cells seeded onto a at least one scaffold, and include a material that functions as a 'semi-permeable membrane' one at least one outer surface of the at least one scaffold. It is noted no specific size or form is required by the method of claim 8, and thus the tissue of claim 13 is not limited in size or form.

Zaleske et al disclose constructs comprised of three cell-seeded (chondrocyte-seeded) cartilage matrices, coated in fibrin glue (See Zaleske et al, col. 5, ln 45-col. 6, ln 11). Each of the cell-seeded cartilage matrices is considered to read on a cell-seeded scaffold, as in the current claims; the fibrin glue forms a 'semi-permeable' membrane around the three cell-seeded matrices (the fibrin glue being permeable to at least the chondrocyte cells), and thus the membrane is present on at least one outer surface of the cell-seeded scaffolds. Because the construct contains living chondrocytes, it is considered to read on 'biological tissue' as claimed. Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zaleske et al (US Patent 6,183,737), in view of Bouhadir et al (Biotechnol Prog. 2001).

Zaleske et al disclose methods of forming a cartilage implant, which reads on the biological tissue as currently claimed. The cartilage implant may be formed by providing two or more non-viable cartilage matrices in apposition, seeding the two or more matrices with isolated chondrocytes to form a cartilage construct, and then applying a biological gel to the cartilage construct to fill gaps at the interface of the two or more cartilage pieces. Alternatively, the individual non-viable cartilage matrices may be seeded with isolated chondrocytes prior to being held in apposition (See Zaleske et al, col. 2, ln 11-33).

In their example, Zaleske et al disclose co-culturing chondrocytes with three non-viable cartilage matrices; loading the cell-seeded matrices onto a sterile Petri dish, such that the three matrices are stacked upon one another; and then applying fibrin glue around the stack of cell-seeded matrices to form a composite cartilage unit (See Zaleske et al, col. 5, ln 45-col. 6, ln 11). The composite cartilage unit is considered to be one and the same as the product of claim 13, as discussed in detail above.

The non-viable cartilage matrices are considered to read on the scaffolds of the instant invention, thus the step of seeding chondrocytes onto the non-viable cartilage matrices reads on the step of 'seeding cells obtained from a tissue to be regenerated onto one or more scaffolds', it is noted the source of the cells (*i.e.* "from a tissue to be regenerated") is a product-by-process limitation and, as discussed above, process limitations are considered only insofar as the method of production imparts distinct structural or chemical characteristics or properties to the product. In the case of the source of the cells, it is noted that source of the cells does not impart any unique structural characteristics to the cells, thus chondrocytes obtained from any source satisfy the limitation of the current claim.

The Petri dish is considered to read on the molding container, having a predetermined size and form, of the instant invention. It is noted the claim does not require the predetermined size and form of the molding container to correlate in any manner to the size and form of the biological tissue being produced, thus, any container to which the scaffolds and other agents are added satisfy this limitation. Thus, the step of loading the cell-seeded matrices into a sterile Petri dish is considered to read on the step of ' loading the scaffold seeded with the tissue cells into a molding container with a predetermined shape and size.'

The exemplified method of Zaleske et al differs from the instant invention in that they apply fibrin glue as the biological gel to adhere the cartilage matrices and to fill gaps at the interface(s) between matrices. While the fibrin glue may be considered a semi-permeable agent that forms a semi-permeable membrane on an outer surface of each of the scaffolds, Zaleske et al does not teach further adding a cross-linking agent, as fibrin does not require cross-linking.

However, it is submitted that, at the time the invention was made, it would have been obvious to one of ordinary skill in the art to alternatively use a calcium alginate gel in place of the fibrin glue, as fibrin glue and calcium alginate gel were both disclosed as suitable biological gels which may be used in the method of Zaleske et al (See Zaleske et al, col. 3, ln 63-col. 4, ln 5). Calcium alginate gel is formed by cross-linking alginate with calcium chloride (See, e.g. Bouhadir et al, Pg. 946, col 1 "Hydrogel Formation and Degradation"), thus to use calcium alginate gel as the biological gel, one would apply alginate, and then calcium chloride to the appositioned scaffolds in the method of Zaleske et al. Alginate reads on the 'semi-permeable agent', calcium chloride reads on the cross-linking agent. Suitability of calcium alginate gel for use with chondrocytes and cartilage implants is further supported by Bouhadir et al. Bouhadir et al disclose using calcium alginate gel (formed by cross-linking alginate with calcium chloride) to

form substrates for culturing chondrocytes (See Bouhadir et al, Pg. 946, col. 1 "Hydrogel Formation and Degradation").

It is further noted that Bouhadir et al report using Teflon molds to form the calcium alginate gels (See Bouhadir et al, pg. 946, col. 1); thus it is submitted that use of Teflon molds as a support structure for holding or otherwise supporting the biological tissue would have been obvious because, again, the substitution of one known element for another (Teflon for Petri dishes) would have yielded the predictable result of successfully holding the construct, thereby rendering the invention obvious to one of ordinary skill in the art at the time the invention was made.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Examiner, Art Unit 1651